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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
097010,317	01/21/98	HOOK	TAMK:189

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EXAMINER
WEATHERSPOON, J

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/010,317

Applicant(s)
Hook et al

Examiner
John K. Weatherspoon

Group Art Unit
1645



☒ Responsive to communication(s) filed on Jun 10, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-53 is/are pending in the application.

Of the above, claim(s) 1-32 and 38-53 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 33-37 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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DETAILED ACTION

1. Applicant's election with traverse of the restriction requirement with regard to Groups I, II and VI in Paper No.10 is acknowledged. Applicants argue the traversal on the grounds that the claims of Groups I and II are related since the peptide of Group II is used to generate the antibody of Group I; and Groups I and VI are related as antibodies and method of generating antibodies and should be examined together "on that basis". Applicants arguments have been fully considered but are not persuasive for the reasons set forth previously. In particular, antibody and peptide are structurally and functionally distinct products; and the antibody of Group I can be made by a materially different process, e.g. by recombinant means. For the reasons of record, because the inventions of Groups I, II and VI are distinct and have acquired a separate status in the art as shown by their different classifications and/or recognized divergent subject matter and because the searches required for examination of the groups identified above are not coextensive, restriction for examination purposes is deemed proper and is therefore made FINAL. In view of applicants provisional election of Group I drawn to claims 33-37, claims 33-37 are under examination. Claims 1-32 and 38-53 have been withdrawn from further consideration by the examiner, according to 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information

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submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsman under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Claim Rejections - 35 USC § 112 first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claimed invention is drawn to methods for generating antibodies that bind to fibronectin binding domain (rFnBD; as referred to by applicants in the instant specification) of a fibronectin binding protein (FBP) and inhibit binding of said FBP to fibronectin (Fn), comprising administering to an animal a composition comprising an isolated peptide of a rFnBD of a FBP,

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“wherein said peptide does not specifically bind to fibronectin”. Unlike the identification of Fn-binding peptides, e.g. microbial surface components recognizing adhesive matrix molecules (as disclosed by applicants in the instant specification) that do bind fibronectin, applicants further disclose in the instant specification (e.g. see page 4 of specification and see McGavin et al, 1991 reference) that amino acid substitution or mutation, e.g. by site-directed mutagenesis techniques or “mutagenizing a plurality of peptides” (page 12 of the instant specification), of Fn-binding peptides must be employed to practice the claimed invention, i.e. to generate a peptide that “does not specifically bind to fibronectin” as claimed. Applicants further disclose that said peptides that do not “specifically bind to fibronectin” are obtained by amino acid mutations, which one skilled in the art recognizes to encompass amino acid additions, substitutions and/or deletions, of wild-type fibronectin binding peptides by, for example, site-directed mutagenesis (e.g. page 10 of the instant specification). However, one skilled in the art recognizes that protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al cited on PTO-892). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (see Lazar et al). These references demonstrate that even a single amino acid substitution or an apparent inconsequential chemical modification will often affect the biological activity of a protein.

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Further, one skilled in the art recognizes that antibodies generated to bind to a fibronectin binding domain of a fibronectin binding protein (FBP) do not predictably or reliably inhibit said binding of said FBP to fibronectin (for example, see Ciborowski et al, 1992). Ciborowski et al disclose that antibodies purified from mice immunized with a beta-D-galactosidase Fn-binding protein (gal-FnBP), i.e. antibodies directed against the Fn-binding region of said gal-FnBP, do *not* block the specific binding of Fn to gal-FnBP in blocking assays (see entire reference).

Applicants specification has provided insufficient guidance for one skilled in the art to predictably obtain peptides that do not “specifically bind to fibronectin”, in view of the teachings above with regard to unpredictability of amino acid mutations on protein biological function. Further, the specification has provided insufficient guidance for one skilled in the art to predictably generate claimed antibodies based upon administration of a composition comprising mutated fibronectin binding peptides. In view of the above teachings, one skilled in the art recognizes that to generate antibodies that inhibit binding of FBP to fibronectin by administering to an animal a composition comprising an isolated peptide of a rFnBD of a FBP, “wherein said peptide does not specifically bind to fibronectin”, as instantly claimed, one skilled in the art would require undue experimentation to practice the claimed invention since, *by applicants instant disclosure*, mutation of Fn-binding peptides is required to generate said peptides that do not specifically bind fibronectin, and further since introducing mutations into wild-type peptides confers unpredictable effects on biological function, e.g “specific” binding activity, of a peptide.

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Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Rozalska et al (1994 reference; see PTO-892). Rozalska et al disclose a method of generating antibodies that bind to a fibronectin binding domain of a fibronectin binding protein (FBP), wherein said antibodies inhibit binding of said FBP to fibronectin (Fn), comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of an isolated peptide of a fibronectin binding domain of a FBP, wherein said peptide does not specifically bind to fibronectin. In particular, Rozalska et al disclose administration, i.e. immunization, of rabbits with an immunologically effective amount of isolated peptides of a fibronectin binding domain of a FBP (e.g., Gal-FnBP A and alb-FnBP A), wherein said peptides display binding sites in addition to binding fibronectin, i.e. said peptides do not specifically bind to fibronectin (see entire reference), and further generation of antibodies that inhibit binding of said Gal-FnBP A and alb-FnBPA to Fn. In view of said disclosure, said claims are anticipated by the prior art.

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Status of Claims

6. No claim is allowed.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1645 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Weatherspoon, Ph.D. whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (703) 308-3995.

John Weatherspoon, Ph.D.

June 30, 1999



Anthony Caputa, Ph.D.

Supervisory Primary Examiner

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